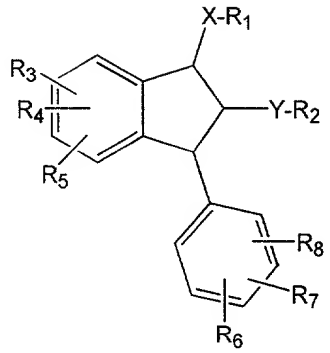
WHAT IS CLAIMED IS:

1. A compound of the formula:



Formula I

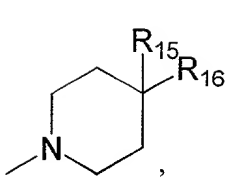
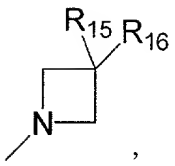
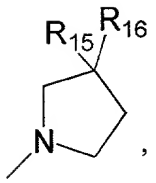
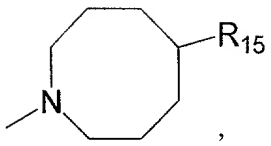
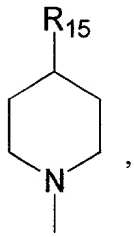
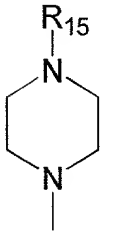
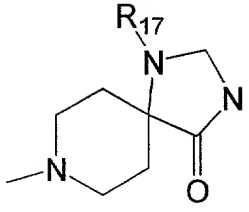
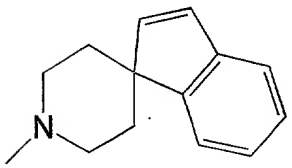
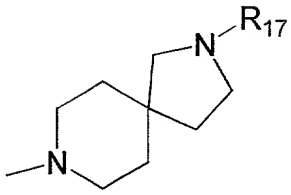
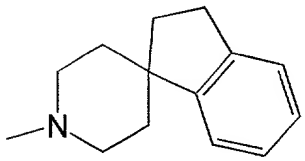
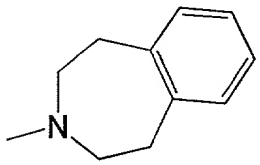
wherein:

R_1 and R_2 are each independently $-OR_9$ or $-NR_{10}R_{11}$;

R_3, R_4, R_5, R_6, R_7, and R_8 are each independently hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{1-10} alkoxy, phenyl, phenoxy, benzyl, benzyloxy, C_{3-8} cycloalkyl, $N(R_{12})_2$, $NHCOR_{13}$, $S(O)_qC_{1-10}$ alkyl, OH, or halogen; wherein C_{1-10} alkyl, C_{2-10} alkenyl, or C_{2-10} alkynyl may be optionally substituted by COOH, OH, $CO(CH_2)_nCH_3$, $CO(CH_2)_n$, $CH_2N(R_{12})_2$, or halogen; or R_3 and R_4, R_4 and R_5, R_6 and R_7, or R_7 and R_8 together may be -O-A-O- on contiguous carbons;

R_9 is C_{1-10} alkylene, C_{2-10} alkenylene, C_{2-10} alkylidene, or C_{2-10} alkynylene, all of which may be linear or branched or phenylene, all of which may be unsubstituted or substituted by one or more OH, COOH, alkoxy, NHR_{12}, $N(R_{12})_2$, $NHCOR_{13}$ or halogen; or R_9 is alkylsilyl, arylsilyl or alkylarylsilyl;

R_{10} and R_{11} are each independently C_{1-10} alkylene, C_{1-10} alkenylene, C_{2-10} alkylidene, C_{2-10} alkynylene, $S(O)_q(R_{14})$, $C(O)NH(R_{14})$, and $C(O)_q(R_{14})$, all of which may be linear or branched, phenylene or benzylene, all of which may be unsubstituted or substituted by one or more OH, COOH, alkoxy, NHR_{12}, $N(R_{12})_2$, $NHCOR_{13}$ or selected from the following group:

R_{12} is hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, benzyl, or aryl, all of which may be unsubstituted or substituted by one or more OH, COOH, NH_2, secondary amine, tertiary amine, tetrazole, or PO_3H_2;

R_{13} is C_{1-10} alkyl, C_{2-10} alkenyl, benzyl, or aryl, all of which may be unsubstituted or substituted by one or more OH, COOH, NH_2, secondary amine, tertiary amine, tetrazole, or PO_3H_2;

R_{14} is C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-6} cycloalkyl, phenyl, and benzyl; wherein C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl maybe optionally substituted by COOH, $CO(CH_2)_nCH_3$ or OH;

R_{15} and R_{16} are each independently hydrogen, aryl, C_{1-10} alkyl, C_{2-10} alkenyl, and C_{2-10} alkynyl, all of which may be unsubstituted or substituted by one or more CH_2OH, $N(R_{12})_2$, $NHCOR_{13}$, OH, or halogen; wherein aryl is naphthyl, indolyl, pyridyl, thienyl, oxazolidinyl, oxazolyl, thiazolyl, isothiazolyl, pyrazolyl, triazolyl, tetrazolyl, imidazolyl, imidazolidinyl, thiazolidinyl, isoxazolyl, oxadiazolyl, thiadiazolyl, morpholinyl, piperidinyl, piperazinyl, pyrrolyl or pyrimidyl, all of which may be unsubstituted or substituted by one or more R_{17}, R_{18}, R_{19}; wherein if R_{15} occurs without R_{16}, R_{15} is not hydrogen;

R_{17}, R_{18}, R_{19} are each independently hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, phenyl, benzyl, C_{3-8} cycloalkyl, C_{1-10}alkoxy, $S(O)_qC_{1-10}$ alkyl, $N(R_{14})_2$, $NHCOR_6$, OH, or halogen; wherein C_{1-10} alkyl, C_{2-10} alkenyl or C_{2-10} alkynyl may be optionally substituted by COOH, $CO(CH_2)_nCH_3$, $CO(CH_2)_n$, $CH_2N(R_{14})_2$, OH or halogen;

X and Y are each independently $-CH_2-$, $-(CH_2)_2-$, $-(CH_2)_3-$, C=O, $CH_2C(O)$, $(CH_2)_2C(O)$, CH_2SO_2, and $(CH_2)_2SO_2$;

q is zero, one, two, or three;

n is an integer from zero to six;

or a diastereomer, enantiomer or pharmaceutically acceptable salts thereof.

2. The compound of claim 1 wherein X is $CH_2(O)$, and Y is C=O.

3. The compound of claim 2 wherein R_3 and R_6 are H; and R_4, R_5, R_7 and R_8 are $-OCH_3$.

4. The compound of claim 3 which is 2-[2-(4-benzylpiperidine-1-carbonyl)-3-(3,4-dimethoxy-phenyl)-5,6-dimethoxy-indan-1-yl]-1-(4-benzylpiperidin-1-yl)-ethanone.

5. The compound of claim 3 which is 2-{3-(3,4-dimethoxyphenyl)-5,6-dimethoxy-2-[4-(2-ethoxyphenyl)-piperazin-1-carbonyl]-indan-1-yl}-1-[4-(2-ethoxyphenyl)-1-yl]-ethanone.

6. The compound of claim 1 wherein X is $-(CH_2)_2-$, and Y is $-CH_2-$.

7. The compound of claim 6 wherein R_3 and R_6 are H; and R_4, R_5, R_7 and R_8 are $-OCH_3$.

8. The compound of claim 1 wherein X is $-(CH_2)_2-$, and Y is $-CH_2-$; R_2 is $-OCH_3$; R_3 and R_6 are H; and R_4, R_5, R_7 and R_8 are $-OCH_3$.

9. The compound of claim 8 which is 1-benzyl-4-{2-[3-(3,4-dimethoxyphenyl)-5,6-dimethoxy-2-methoxymethyl-indan-1-yl]-ethyl}-piperazine.

10. A method of inhibiting P-glycoprotein-mediated transport, the method comprising administering a compound of Formula I.

11. The method of claim 10 wherein the compound of Formula I is selected from the group presented in Table I.

12. The method of claim 11 wherein the compound has a percentage inhibition of Rhodamine 123 transport of at least 30%.

13. The method of claim 12 wherein the compound has a percentage inhibition of Rhodamine 123 transport of at least 50%.

14. The method of claim 13 wherein the compound has a percentage inhibition of Rhodamine 123 transport of at least 80%.

15. The method of claim 11 wherein the compound of Formula I is coadministered with a pharmaceutical compound.

16. The method of claim 15 wherein the coadministered pharmaceutical compound has a percentage increase in cytotoxicity value of at least 30%.

17. The method of claim 16 wherein the coadministered pharmaceutical compound has a percentage increase in cytotoxicity value of at least 50%.

18. The method of claim 17 wherein the coadministered pharmaceutical compound has a percentage increase in cytotoxicity value of at least 80%.

19. Use of a compound of Formula I as an inhibitor of P-glycoprotein-mediated transport.

20. An inhibitor of P-glycoprotein-mediated transport comprising a compound of Formula I.

21. A method of increasing bioavailability of an orally administered pharmaceutical compound, the method comprising:

orally coadministering (1) the pharmaceutical compound to a mammal in need of treatment with the pharmaceutical compound and (2) a compound of Formula I in an amount of the compound of Formula I sufficient to provide bioavailability of the pharmaceutical compound in the presence of the compound of Formula I greater than bioavailability of the pharmaceutical compound in the absence of the compound of Formula I.

22. A method of treating multidrug resistance in mammals, the method comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Formula I.

23. A composition for inhibition of P-glycoprotein-mediated transport in mammals, the composition comprising a compound of Formula I in a pharmaceutically acceptable carrier.

24. A method of treating a tumor, the method comprising coadministering to a mammal in need thereof a therapeutically effective amount of a compound of Formula I and a therapeutic agent.

25. The method of claim 23 wherein the tumor is drug-resistant.

26. The method of claim 23 wherein the tumor has converted from drug-sensitive to drug-resistant.

27. The method of claim 23 wherein the therapeutic agent is a P-glycoprotein substrate.

28. The method of claim 23 is selected from doxorubicin, vinblastine, vincristine, epipodophyllotoxin, taxanes, paclitaxel, docetaxel, etoposide, tenopiside, colchicines, daunorubicin, topotecan, actinomycin D, mitoxantrone, mitomycin C.

29. A method of preventing multidrug resistance in tumor cells, the method comprising administering an effective amount of a compound of Formula I to the tumor cells.

30. A method of treating a tumor, the method comprising administering to a mammal in need thereof a therapeutically effective amount of a composition, the composition including a therapeutic agent and a compound of Formula I.

31. A method for increasing the sensitivity of tumor cells that have converted from sensitivity to therapeutic agents to resistance to the therapeutic agents, the method comprising coadministering to a mammal a therapeutically effective amount of a compound of Formula I and at least one of the therapeutic agents.

32. A pharmaceutical composition for increasing the sensitivity of tumor cells that have converted from sensitivity to therapeutic agents to resistance to the therapeutic agents, the pharmaceutical composition comprising (1) a therapeutically effective amount of a compound of Formula I, (2) at least one of the therapeutic agents, and (3) a pharmaceutically acceptable carrier.

33. A method of converting a non-orally bioavailable pharmaceutical composition into an orally bioavailable pharmaceutical composition, the method comprising formulating a composition including a compound of Formula I and the non-orally bioavailable pharmaceutical composition and optionally a pharmaceutically acceptable carrier.

34. An orally bioavailable pharmaceutical composition produced by the method of claim 33.

35. A method of delivering a pharmaceutical compound to the central nervous system of a patient, the method comprising coadministering the pharmaceutical compound with a compound of Formula I.